

## REMARKS

As a result of the present amendment, claims 1-6, 15-16 have been amended. The species added in claim 15 find support on pages 15, 36 and 92. The species removed from claim 16 did not have the R4 aspect common to all other species and was therefore deleted. Claims 1-16 are pending in this application. No new matter has been added to this application by way of amendment.

## CLAIM REJECTIONS

Claims 1-9 have been rejected under 35 USC 112 second paragraph as allegedly being indefinite.

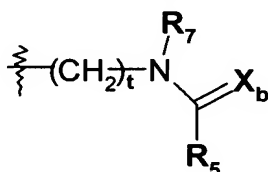
Applicants have amended claims 1-6 to address the issues raised in the office action. Withdrawal of the 35 USC 112 second paragraph rejection is therefore respectfully requested.

Claims 1-9, 15-16 have been rejected under 35 USC 103(a) as allegedly being unpatentable over Frenkel et al. (US 2003/0144286), Craig et al. (US 3,336,191), Craig et al. (US 3,401,171), and Smith Kline & French Labs (GB 1,122,957) each taken alone or in combination. This rejection is traversed.

Applicants contend that the prior art of record, either alone or in combination, does not teach or suggest all the limitations of the instant claims for all the reasons set forth on the previous paper, and the following.

Applicants submit herewith the declaration of Hidenori Takahashi. The declaration presents evidence of unexpected results in anti-ITK activity observed for the particular combination of structural features provided by the claimed compounds. The data reports the IC<sub>50</sub> (*nM*) of ITK (inhibitory concentration in *nM* to obtain 50% inhibition of ITK) using the ITK assay found on page 143 of the present patent application. The declaration

accordingly provides a direct comparison of the anti-ITK activity of several of the claimed compounds versus the closest cited prior art compounds. Specifically, the critical structural features of the compounds of the invention are when the **R<sub>4</sub>** moiety is



and the **R<sub>3</sub>** group is :  $-(CH_2)_n-L-R_6$ . This is neither taught nor suggested by the prior art of record. Moreover, the closest prior art compounds disclosed by Frenkel et al do not suggest applicants' selection invention wherein **R<sub>6</sub>** is any cyclic group, then **R<sub>6</sub>** is not directly attached to the benzimidazole nitrogen by virtue of **n** being a minimum of 1. In contrast, the closest compounds by Frenkel et al to the instant compounds exemplify compounds possessing IRAC activity, wherein the analogous **R<sub>6</sub>** cyclic group is directly attached to the benzimidazole nitrogen. In the table presented in the declaration, it can be seen that the compounds of the invention resulted in a significant increase in inhibition over the closest compounds of each prior art reference. The observed improvement of anti-ITK activity by the particular combination of structural features provided by the claimed compounds is nowhere disclosed or suggested in the prior art of record, and provides evidence of surprising and unobvious results in rebuttal to any prima facie case of obviousness. Accordingly, the claimed invention is believed to be unobvious from the prior art of record, and accordingly withdrawal of the rejection under 35 USC § 103 is respectfully requested.

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